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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,695	07/20/2001	Joseph A. Hedrick	DX0757K	2825

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EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/910,695	Hedrick et al.
Examiner	**Art Unit**
Prema Mertz	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Nov 1, 2002*.

2a) ☐ This action is **FINAL**. 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *11-19, 22-27, and 37-40* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *11-19, 22-27, and 37-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) X Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s).
2) X Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application (PTO-152)
3) X Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6	6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicants election with traverse of Group VII (claims 11-19, 22-27 and new claims 37-40) in Paper No. 8 (11/1/02) is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP.. § 818.03(a)).

Furthermore, Applicants cancellation of claims 1-10, 20-21 and 28-36 renders the traversal of the restriction requirement moot.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed because the claims are directed to a nucleic acid and the title recites the protein.

Appropriate correction is requested.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 19 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claim embraces a use of the claimed nucleic acid and there are no provisions for "a use" in the statutes. Amending the claim to delete the recitation of "using" and to

recite "a process or a method" will obviate this rejection, but does not prevent the Examiner from making the next office Action final.

In view of the improper format for claim 19, this claims will be examined for a reasonable interpretation of its intended meaning.

4. Claims 12-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims embrace a host cell in the body of a transgenic animal, or a host cell in a gene therapy patient. Claims 12-13 encompass human cells, fetuses and embryos, as well as non-human cells including animals, vertebrates, mammals, primates, chimeric animals, germ cells (including oocytes and sperm), fertilized eggs, fetal tissues and organs. However, since it would that applicants do not intend to claim such human cells, amending the claims to require non-human host cells and the hand-of-man would obviate this rejection i.e. an isolated non-human mammalian host cell.

5. Claims 11-19, 22-27, 37-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein, BLRx, identified in the specification as having homology to various G-protein coupled receptors" (page 12, lines 27-34), the instant invention is incomplete. The translation product of the protein encoded by the claimed nucleic acid, shares sequence homology with the "bovine gustative receptor" (see specification page 12, lines 31-34). However, the instant

specification does not disclose any information regarding functional characteristics or the biological activity of the instantly claimed nucleic acid encoding the primate BLRx protein. While the specification on page 5, lines 30-37 and page 6, lines 1-2 discloses that the receptors are typically G-protein coupled receptors (GPCR), there is no guidance given about which specific ligand the claimed nucleic acid encoding the polypeptide would be likely to bind to. The specification does not demonstrate that the claimed nucleic acid encoding a polypeptide actually displays any of the activities of a GPCR. In the absence of knowledge of the specific biological significance of the claimed nucleic acid encoding a protein, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for the nucleic acid encoding the protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

A protein of unknown function would have utility if it can be employed as an indicator of a diseased state or of the presence of a disorder. The only disclosed function for the protein of the instant invention is that it has homology to the bovine gustative receptor (see page 12, lines 31-34). However, Applicants have failed to show that the instant protein is a member of the GPCR family and that the protein has a specific function. The Examiner's position is that this member of the GPCR family does not have a specific utility because different receptors have different functions and the specific function of this particular receptor has not been demonstrated in the instant application.

Applicant is only required to identify one substantial credible utility and the employment of this protein only as the subject of further research does not satisfy the utility requirement of 35 U.S.C.

§ 101 because the courts have interpreted this statute as requiring an invention to have "substantial utility" "where specific benefit exists in currently available form". The disclosure that the nucleic acid of the instant invention encodes a GPCR protein, is not a substantial or specific utility.

Applicants disclose in the specification that the protein has homology to the bovine gustative receptor (see page 12, lines 31-34). However, Applicants have failed to disclose what specifically the instant receptor does. What is the physiological activity of the polypeptide of the instant invention? The state of the art is such that functional information can be automatically derived from structural information only to a limited extent, (see Sklonick et al, Nature Biotechnology, Vol.18, No.3, pages 283-287, especially page 286, middle of column 1). Sklonick et al also state that knowledge of the overall structure or domain family is still not enough to confidently assign function to a protein. Therefore, there is little doubt that, after further characterization, the protein is found to be member of the decay accelerating factor family, the claimed protein would have a specific, substantial and credible utility. However, further characterization is part of the invention and until it had been undertaken, the claimed invention is not supported by a specific asserted utility or a well established utility. The claimed invention is directed to a nucleic acid encoding a polypeptide of as yet undetermined function or biological significance. Thus, since there is no biological activity disclosed for the protein encoded by the claimed nucleic acid, the claimed invention is not supported by either a specific and substantially asserted utility or a well established utility.

Claims 11-19, 22-27, 37-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or

a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed nucleic acid encoding a protein, therefore, there is no specific and substantial asserted utility or well established for the claimed nucleic acid encoding a protein. The fact that the claimed nucleic acid encodes a protein that has homology to the bovine gustative receptor (see page 12, lines 31-34) is not sufficient to establish a specific and substantially asserted utility or a well established utility for it.

Should Applicants establish an activity for the polypeptide of SEQ ID NO: 8 encoded by the polynucleotide of SEQ ID NO: 7, the instant specification would still fail to adequately describe and enable an isolated protein that is at least about 80 % identical to the polypeptide of SEQ ID NO:8. Applicants do not teach which regions of said polypeptide are critical to encode a functional polypeptide. The specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce a polypeptide having at least 80% sequence identity to SEQ ID NO:8, nor does the disclosure provide criteria that explicitly enable such critical features. There is no guidance in the specification as to how one of ordinary skill in the art would generate a polypeptide, other than that exemplified. The issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record.

In summary, the amount of experimentation required for one of ordinary skill in the art to use the claimed invention, an isolated nucleic acid encoding a polypeptide that is at least 80 % identical to the polypeptide of SEQ ID NO:8, would be undue. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those nucleotide sequences of the disclosed naturally-occurring nucleic acid encoding the polypeptide, which are required for functional and structural integrity of the claimed polypeptide. It is this additional characterization of the disclosed polypeptide that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

Claim rejections-35 U.S.C. 112, first paragraph

5a. Claims 22-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 22-23 are genus claims. Claims 22-23 encompass nucleic acid molecules encoding protein variants of SEQ ID NO:8. The term variant means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to the protein molecule of amino acid sequence set forth in SEQ ID NO:8. The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the nucleic acid molecule. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid encoding a protein set forth in SEQ ID NO:8 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicants were not in possession of the claimed genus of nucleic acid molecules encoding protein molecules.

Therefore only an isolated nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:8, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. As a result, it does not appear that the inventors were in possession of variants of a nucleic acid encoding polypeptide of SEQ ID NO:8.

5b. Claims 22-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:8, does not reasonably provide enablement for a peptide as set forth in claims 22-23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 22-23 encompass nucleic acid variants and nucleic acid molecules encoding polypeptide variants of the amino acid sequence set forth in SEQ ID NO:8, which claims are overly broad, since no guidance is provided as to which of the myriad of nucleic acid molecules encompassed by the claims will retain the characteristics of those desired. Variants of the nucleic acid can be generated by conservative or nonconservative changes, allelic, splice species or polymorphic variants. However, Applicants have failed to disclose any actual or prophetic examples on expected performance parameters of any of the possible peptide muteins of SEQ ID NO:8. Moreover, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration

inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate nucleic acid molecules encoding polypeptides other than those exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the

invention based on the content of the disclosure. Given the breadth of claims 22-23, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 24-27 are rejected under 35 U.S.C. 112, first paragraph, insofar as they depends on claims 22-23 for their limitations.

Claim rejections-35 USC § 112, second paragraph

6. Claims 15-19, 22-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-23 are rejected as vague and indefinite in their recitation of the limitation "about 80%...". The term "about" is unacceptably vague and indefinite since it unclear if Applicants intend to claim "85%", "90%" or even "95%" identity.

Claim 15 is indefinite in the recitation of "less than 700 mM salt". This language is vague and indefinite since it encompasses potentially any wash solution, even one without any salt. Therefore, the metes and bounds of the claim are unclear. Similarly claims 16-17 are unclear because it cannot be determined if the wash conditions are with or without salt.

Claims 18-19 and 24-27 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim rejections-35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuoka et al. (1993).

Matsuoka et al. teach cDNAs and the amino acid sequences of the encoded G-protein coupled receptors expressed in mammalian taste tissue (see page 505, paragraph 4; Figure 1, on page 506,; and Figure 3 on page 509). A copy of the comparison of SEQ ID NO:8 claimed in the instant invention and the amino acid sequence of one of the G-protein coupled receptor type B of the reference is enclosed at the end of this action (SEQUENCE COMPARISON A). Therefore, the nucleic acid disclosed in the reference encoding a polypeptide (from amino acid 6-19 of the reference) exhibiting a length of at least 14 amino acids in common with SEQ ID NO:8 of the instant invention, meets the limitations of instant claim 15. Furthermore, with respect to claims 16-17, 19, the cDNA of the reference would be capable of hybridizing to the polynucleotide of SEQ ID NO:7 described in the instant application, under the conditions recited in claims 16-17, and would produce a duplex nucleic acid by contacting one strand of the nucleic acid to the complementary strand. Therefore, the cDNA disclosed in the reference meets the limitations of claims 15-17, 19.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 305-3014 or (703 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
December 23, 2002